

**IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION**

ERFINDERGEMEINSCHAFT UROPEP
GbR,

Plaintiff,

V.

ELI LILLY AND COMPANY, and
BROOKSHIRE BROTHERS, INC.,

Defendants.

Case No. 2:15-CV-1202-WCB

MEMORANDUM OPINION AND ORDER

On June 23, 2016, the Court held a hearing to address the proper construction of the disputed terms of the patent at issue in this case, U.S. Patent No. 8,791,124 (“the ’124 patent”). After considering the arguments made by the plaintiff Erfindergemeinschaft Uropep GbR (“Uropep”) and defendants Eli Lilly and Company, and Brookshire Brothers, Inc. (collectively, “Lilly”) both at the hearing and in their claim construction briefing (Dkt. Nos. 105, 105, and 109), the Court issues this order setting forth the Court’s construction of three of the claim terms identified by the parties. The Court will postpone construction of the fourth claim term, “an inhibitor of phosphodiesterase,” until the Court rules on Lilly’s motions for summary judgment, Dkt. Nos. 119 and 120.

The '124 patent is entitled “Use of Phosphodiesterase Inhibitors in the Treatment of Prostatic Diseases.” Its three claims are directed to methods for prophylaxis or treatment of benign prostatic hyperplasia (“BPH”), or an enlarged prostate, a condition that affects men, typically after the age of 50.

The specification of the '124 patent explains that BPH can result in difficulty in urination because the increase in the size of the prostate gland can impede the passage of urine from the bladder. In the development of BPH, the muscular portions of the prostate increase substantially in volume. It was discovered that a significant improvement in the condition could be achieved by the administration of drugs that result in relaxation of the prostate muscle cells. Prior art treatments, such as the use of alpha-receptor blockers, were characterized by low effectiveness, slow onset of action, or significant side effects. It was discovered, however, that more successful outcomes could be obtained by suppressing phosphodiesterase, an enzyme within the smooth muscles of the prostate gland. '124 patent, col. 1, ll. 9-35.

The specification explains that the body's transmission of information that causes the relaxation of smooth muscle cells is effected through either hormones or neurotransmitters. Such transmission causes an increase in the levels of two cyclic nucleotides, cyclic adenosine monophosphate ("cAMP") and cyclic guanosine monophosphate ("cGMP") in the smooth muscle cells, which in turn promotes the relaxation of those cells. The relaxation of the smooth muscles cells in the prostate reduces the pressure on the bladder and urethra, alleviating the effects of BPH.

The specification states that it was known in the early 1990s that cAMP and cGMP are hydrolyzed (i.e., broken down) by phosphodiesterases ("PDEs"). Researchers discovered that inhibitors of PDEs counteracted that process and thereby reduced the digestion of cAMP and cGMP, allowing those nucleotides to continue promoting the relaxation of the smooth muscle cells. '124 patent, col. 1, ll. 36-52. It was also known that there are a number of subesterases of PDE and that those subesterases are differently distributed in individual organs and organ systems. Id., col. 1, ll. 53-65.

The specification notes that three of those subesterases of PDEs—sPDE I, sPDE IV, and sPDE V—are of particular importance in human prostatic muscles. '124 patent, col. 2, ll. 6-11. The specification states that “[a] well-aimed inhibition of these isoenzymes will result in relaxation of the prostatic muscles even when minute doses of a specific inhibitor are administered, with no appreciable effects in other organ strips, in particular vessels, being observed.” Id., col. 2, ll. 11-14.

The three claims of the '124 patent are directed to methods of treatment of BPH involving the administration of inhibitors of the specific subesterase PDE V. Claim 1 recites administering an effective amount of an inhibitor of PDE V, other than eight named compounds and their pharmacologically compatible salts. Claim 2 recites the method of claim 1 in which the particular inhibitor compound is 2-(2-propoxyphenyl)-8-azapurin-6-one or a pharmacologically compatible salt thereof. Claim 3 recites the method of claim 1 wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.

The claim construction disputes between the parties are all directed to claim 1 of the '124 patent. That claim reads as follows, in pertinent part:

A method for prophylaxis or treatment of benign prostatic hyperplasia comprising administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected for the group consisting of [eight identified compounds] and pharmacologically compatible salts thereof.

The Court will address the parties' disagreement about the proper construction of three terms from that claim: “administering”; “a person in need thereof”; and “an effective amount.”

1. “administering”

Uropep argues that the term “administering” means “giving, providing, prescribing, dispensing, dosing, self-dosing, or taking.” Lilly argues that the term has its plain and ordinary meaning as understood by a person of ordinary skill in the art and needs no construction.

The Court is dissatisfied with both parties’ proposed constructions of the term “administering.” As for Lilly’s suggestion that the term needs no construction, it has become clear in the course of this litigation that the parties have a different concept of what constitutes “administering” a drug.¹ The difference in the parties’ view is clearest as it relates to the potential liability of defendant Brookshire Brothers, Inc., which operates pharmacies that dispense Cialis. The dispute between the parties over the meaning of the term “administering” relates to whether, and under what circumstances, a pharmacist may be considered to “administer” a drug that is provided to a patient for treatment.

Under these circumstances, for the Court to decline to construe the term “administering” would risk creating a situation in which the parties would present differing interpretations of the term to the jury and the jury would in effect be called upon to construe the term. That would be contrary to the Federal Circuit’s admonition in O2 Micro International, Ltd. v. Beyond Innovation Technology Co., 521 F.3d 1351, 1362 (Fed. Cir. 2012), where the court explained that “[w]hen the parties present a fundamental dispute regarding the scope of a claim term, it is the court’s duty to resolve it.” See also Eon Corp. IP Holdings v. Silver Spring Networks, 815 F.3d 1314 (Fed. Cir. 2016).

¹ The parties’ briefing in both Brookshire’s Motion to Dismiss (Dkt. No. 27) and Lilly’s Motion to Sever and Stay and Transfer (Dkt. No. 28) made clear that “administering” was a central dispute in the case and that the parties had different conceptions of its meaning.

A few courts have construed the term “administering” in the context of administering a drug to a patient. The closest case identified by the parties or this Court is Accorda Therapeutics Inc. v. Apotex Inc., Civil Action No.07-4937, 2011 WL 4074116 (D.N.J. Sept. 6, 2011). In that case, the court construed the term “administering” to mean “giving, prescribing, dispensing, dosing, self-dosing or taking.” Accorda, Civil Action No. 07-4937, at *2 (D.N.J. July 2, 2010). In light of that construction, the court concluded that a pharmacist could be regarded as administering a drug; as the court put it, “a physician, pharmacist, or patient could alone infringe the patent.” Id. at *27.

Other courts, although not addressing the question whether a pharmacist “administers” the medicine that the pharmacy dispenses, have adopted similar language in defining the term “administering” as that term is used in medical treatment patents. See Identix Pharms., Inc. v. Gilead Scis., Inc., Civil Action No. 13-1987 et al., at 15 (D. Del. Dec. 16, 2015) (defining “administering” as “making available”); MSD Consumer Prods., Inc. v. Par Pharm., Inc., Civil Action No. 10-4837, at 1 (D.N.J. Oct. 16, 2013) (“The term ‘administering’ . . . shall be construed according to its ordinary and accustomed meaning . . . (e.g. to mete out, dispense, or give remedially).”); Bristol-Myers Squibb Co. v. Apotex, Inc., Civil Action No. 10-5810, 2013 WL 1314733, at *10-11 (D.N.J. Mar. 28, 2013) (construing “administering” to mean “to mete out or dispense or to give remedially”); cf. AstraZeneca AB v. Ammi USA, Inc., No. Civ. 11-760, 2012 WL 6203602, at *5 (D.N.J. Dec. 12, 2012), aff’d, 554 F. App’x 912 (Fed. Cir. 2013) (“oral administration” is not limited to “the prescription by a physician or other licensed healthcare professional, dispensing and ingestion,” but would be understood by a person of ordinary skill in the art to refer to the means of delivering the medication to an individual).

Dictionary definitions of the term “administer” are generally similar. In the context of medical treatment, standard dictionaries define the term “administer” to mean “to give remedially,” Webster’s Third New Int’l Dictionary 27 (2002); Merriam-Webster’s Collegiate Dictionary 16 (11th ed. 2003) (same); “to apply as a remedy,” American Heritage Dictionary 22 (4th ed. 2000); “to give as a remedy,” Webster’s II New College Dictionary 15 (3d ed. 2005); and “to give somebody a measured amount of a medication, often also physically introducing it into the body,” Encarta World English Dictionary 20 (1999).

While Uropep’s proposed construction of the term “administering” is in some respects consistent with the judicial constructions of “administering” and the dictionary definitions of “administer,” the Court considers Uropep’s proposed construction to be too broad. In particular, Uropep’s position that “administering” includes “giving,” “providing,” or “dispensing” would lead one to conclude that a person is “administering” a drug simply by conveying or providing the drug to another.

That would mean, for example, that the cashier at a drugstore could be considered to “administer” a drug (e.g., aspirin) that he or she hands to a patient, even if the cashier has had no involvement in the actual treatment of the patient other than to provide the drug to the patient, in response to the patient’s request. It would even suggest that, in the case of medicine delivered by mail that the postal carrier is “administering” the medicine because he or she is “providing” it to the patient. Such a construction would go well beyond the ordinary understanding of the term “administering” by a person of ordinary skill in the art.

A person of ordinary skill would contemplate that the person “administering” the drug is involved in the actual treatment of the patient (i.e., forming of a diagnosis for a health issue, devising a course of action to ameliorate that issue, or causing that course of action to be

followed). An individual can be involved in the actual treatment of the patient either by directing the treatment (i.e., issuing instructions to the patient or a third party to carry out the remedial course of action) or by applying the treatment to the patient personally. Thus, “administering” requires some actual involvement in the treatment process, either by supervision or direct involvement in the treatment, which is what appears to be implied by the dictionary definition of “administer” as “to give remedially.” While it is clear that a physician who directs a patient to take a drug in pill form can be said to be “administering” the drug to the patient even if the physician does not actually place the pills in the patient’s mouth, a grocery store clerk who sells a customer a bottle of aspirin upon the customer’s request is not “administering” the aspirin under any relevant understanding of the term.

Accordingly, the Court concludes that an actor must, in some measure, be involved in the actual treatment of the patient, either directly or vicariously, in order for the actor to be considered to be “administering” the drug or other treatment. Based on that ordinary understanding of the term “administering” in the context of giving medical treatment to a patient, the Court construes the term “administering” to mean **“providing treatment, such as by implementing a course of action to ameliorate a health issue; “administering” treatment can take the form of personally causing that course of action to be carried out, or by directing or supervising the treatment (i.e., issuing instructions to another to carry out the course of action to ameliorate the issue). In the case of the administration of drugs, ‘administration’ includes direction and control over the use of the drug or the decision to use the drug.”**

2. “a person in need thereof”

Uropep argues that the phrase “a person in need thereof” should be given its plain and ordinary meaning and needs no construction. Lilly argues that the term is indefinite in the context of the claimed method for “prophylaxis” of BPH.

The phrase “a person in need thereof” appears frequently in patents on pharmaceutical products and methods of treatment.² The role played by the phrase is typically to state that the drug is intended to treat persons who are in need, or deemed to be in need, of treatment for a particular condition. It is equivalent to saying that the patient is being given the drug “for” a particular condition, and as such is entirely unobjectionable on indefiniteness grounds.

In the ’124 patent, the claims provide that the PDE V inhibitor is administered to a “person in need thereof” for “prophylaxis or treatment.” Lilly does not contend that the phrase “person in need thereof” is indefinite as applied to treatment. It argues, instead, that the phrase is indefinite as applied to prophylaxis.

Based on a medical dictionary, Lilly argues that prophylaxis is limited to measures taken to prevent the onset of a disease or condition, and that it does not include measures that are designed to prevent or slow the progression of a disease or condition once it has been contracted. See Steadman’s Medical Dictionary 1575 (28th ed. 2000) (defining prophylaxis as “prevention of disease or of a process that can lead to disease”). A different medical dictionary gives a somewhat broader definition for the term “prophylaxis, defining the term as “prevention of or protective treatment for disease.” American Heritage Medical Dictionary 670 (2007). Uropep’s expert, Dr. Steven A. Kaplan, stated that in the context of the ’124 patent, a person of ordinary skill in the art would understand that a person in need of prophylaxis for BPH “would be a

² The term “effective amount” has appeared in the claims of more than 5000 issued patents during the past 10 years.

person in need of the prevention of the progression or development of BPH and the signs and symptoms secondary to BPH.” Dkt. No. 99-1, at 9.

The Court credits Dr. Kaplan’s testimony and declines Lilly’s invitation to construe “prophylaxis” to be limited exclusively to prevention of the incurrence of a disease or condition. The Court notes that the word “prophylaxis” in the claims is only one half of the larger phrase “prophylaxis or treatment.” As Dr. Kaplan explained in his deposition, at the time of the invention, there was disagreement among physicians as to when a man who has experienced prostate growth would be said to have BPH. See Dkt. No. 106-11, at 20, 27-28. For that reason, there was no clear distinction between prophylaxis and treatment for BPH. Id. at 28. Accordingly, a course of medication designed to deal with the condition could be regarded as either prophylaxis or treatment, depending on the physician’s judgment as to whether the patient has BPH or merely has risk factors for BPH or has at least one of the symptoms of BPH. See Dkt. No. 99-1, at 9-10. In the latter case, Dr. Kaplan explained, “prophylaxis would be desirable to alter or delay the arc of the disease’s progression and, in consequence, to delay the worsening of the symptoms secondary to BPH.” Id. at 10. At the time of the invention, Dr. Kaplan added, that the drugs then used to treat BPH could also be used to prevent the development or progression of BPH. Id.

Dr. Kaplan’s explanation of the uncertain line between prophylaxis and treatment is not unique to BPH. For example, cardiologists often prescribe a daily aspirin regimen for patients whose risk factors, such as family history and prior cardiac irregularities, put them at risk of a heart attack. In that setting, the aspirin regime can be regarded as either treatment of the patient’s cardiac condition or prophylaxis against a cardiac event. This uncertainty might have the potential to create a categorical difficulty if one had to determine whether the regime was

either treatment or prophylaxis. But because the patent claims at issue in this case cover both prophylaxis and treatment, the overlapping nature of the two terms is not problematic.

Based on Dr. Kaplan's declaration and testimony, the Court finds that the term "prophylaxis," as used in the context of medical approaches to BPH at the time of the invention, referred to the prevention of the progression or development of the disease, and that a physician would determine whether a particular patient was a "person in need of" treatment or prophylaxis for BPH depending on the particular patient's signs and symptoms as well as his risk factors for BPH.

The Court thus concludes that the phrase "a person in need thereof" is not indefinite. If a physician administers a particular drug to a patient because the physician concludes that the patient needs the drug, either to prevent or treat BPH, then the drug is being administered to "a person in need thereof," at least absent evidence that the physician's judgment as to the patient's need is wrong under either category. Because the Court concludes that the term "a person in need thereof" is sufficiently clear, not only to persons of skill in the art, but also to laymen, the Court concludes that the phrase is not indefinite even in the context of prophylaxis of BPH. See Nautilus, Inc. v. Biosig Instr., Inc., 134 S. Ct. 2120 (2014). **The Court concludes that the term "person in need thereof" needs no construction. The Court defines the term "prophylaxis" to mean "prevention of the progression or development of the disease."**

3. "an effective amount"

Uropep argues that the term "an effective amount" should be given its plain and ordinary meaning and needs no construction. Lilly argues that the term is indefinite in the context of the claimed method, once again with particular focus on the term "prophylaxis."

The term “an effective amount” is frequently found in pharmaceutical patents,³ as the Federal Circuit has recognized. See Geneva Pharms., Inc. v. GlaxoSmithKline PLC, 349 F.3d 1373, 1383-84 (Fed. Cir. 2003) (the term “effective amount” is “a common and generally acceptable term for pharmaceutical claims”). The Court of Customs and Patent Appeals rejected a challenge to the use of the term “effective amount,” stating that the term “is not objectionable where the *amount* is not critical, and its use has been approved in many cases.” In re Halleck, 422 F.2d 911, 914 (C.C.P.A. 1970). The amount is plainly not critical to the invention of the ’124 patent, as the patent in effect claims a method of treating or preventing BPH through the administration of inhibitors of PDE V, without regard to the specific amount of the inhibitor that is administered in particular cases. The use of the term “effective amount” therefore does not render the claims of the ’124 patent fatally indefinite.

As in the case of the “persons in need thereof” limitation, Lilly’s indefiniteness argument is focused on the use of the term “prophylaxis” in the ’124 patent. Lilly argues that it is impossible to know what amount of the drug is “an effective amount” to achieve prophylaxis, and for that reason the term “effective amount” is indefinite in the context of the ’124 patent, even if the term is ordinarily not objectionable on indefiniteness grounds.

To the extent that Lilly objects to Uropep’s definition of the term “prophylaxis” to mean prevention and amelioration of a condition, the Court disagrees with Lilly, for the reasons set forth above. Thus, the term “an effective amount,” as used in the ’124 patent, refers to the amount that is effective for a particular patient in preventing, ameliorating, or otherwise treating BPH.

³ The phrase “a person in need thereof” has appeared in the claims of more than 27,000 issued patents during the past 10 years.

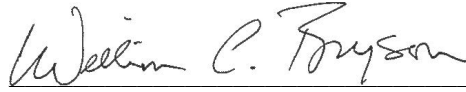
The amount of the PDE V inhibitor that is necessary to treat BPH is not specified in the '124 patent. The point of novelty of the claimed invention, however, is not the particular amount of the dosage, but rather the use of PDE V inhibitors to treat or prevent the disease. Thus, as explained by the court in Halleck, the amount of the dosage is not critical; it can be ascertained on a case-by-case basis for particular patients. As for Lilly's argument that it is impossible to know what dosage would be appropriate for prophylaxis of BPH, Dr. Kaplan stated that a person of ordinary skill "would also understand that 'an effective amount' of a drug to prevent a disease would be the same amount of that drug used to treat the same disease." Dkt. No. 99-1, at 13; see also Dkt. No. 106-11, at 30 ("Our thought process in 1997, which is why we used the doses that were used commonly to treat symptoms, would be the same doses we would look at to prevent or prophylax."). That testimony was uncontradicted by Lilly, which did not offer expert testimony with respect to the claim construction disputes. The Court credits Dr. Kaplan's testimony that the "effective amount" would ordinarily be the same for treatment and prophylaxis.

Moreover, the patent is not entirely silent as to the effective amount of PDE V inhibitor that could be used for treatment or prophylaxis. It contains two in vitro examples in which identified concentrations of a PDE V inhibitor were used. '124 patent, col. 6, line 65, through col. 7, line 34. The Court therefore finds that the term "an effective amount" is not indefinite in the context of the '124 patent and that the use of the term "prophylaxis" in the claims also does not render the "an effective amount" limitation indefinite.

Accordingly, the Court concludes that the meaning of the term "an effective amount" in the '124 patent claims would be reasonably clear to a person of skill in the art and therefore is not indefinite. **The Court concludes that the term "an effective amount" needs no construction.**

IT IS SO ORDERED.

SIGNED this 11th day of August, 2016.

A handwritten signature in black ink, reading "William C. Bryson". The signature is written in a cursive style with a horizontal line underneath the name.

WILLIAM C. BRYSON
UNITED STATES CIRCUIT JUDGE